

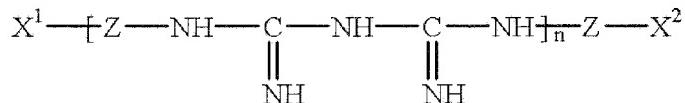
Amendments to the Specification:

Please replace the title of the invention with the following amended title:

IMPROVED OPHTHALMIC AND CONTACT LENS SOLUTIONS WITH A PEROXIDE SOURCE AND A CATIONIC POLYMERIC PRESERVATIVE

Please replace paragraph [0014] of the specification with the following amended paragraph:

[0014] Most preferred are the polymeric hexamethylene biguanides, commercially available, for example, as the hydrochloride salt from Zeneca (Wilmington, Del.) under the trademark ~~Cosmoeil~~TM CQ COSMOCIL CQ. Such polymers and water-soluble salts are referred to as polyhexamethylene (PHMB) or polyaminoptopyl biguanide (PAPB). The term polyhexamethylene biguanide, as used herein, is meant to encompass one or more biguanides having the following formula:



wherein Z, X¹ and X² are as defined above and n is from 1 to 500.

Please replace paragraph [0025] of the specification with the following amended paragraph:

[0025] A typical aqueous solution of the present invention may contain additional ingredients which would not affect the basic and novel characteristics of the active ingredients described earlier, such as tonicity agents, surfactants and viscosity inducing agents, which may aid in either the lens cleaning or in providing lubrication to the eye. Suitable tonicity agents include sodium chloride, potassium chloride, glycerol or mixtures thereof. The tonicity of the solution is typically adjusted to approximately 240-310 milliosmoles per kilogram solution (mOsm/kg) to render the solution compatible with ocular tissue and with hydrophilic contact lenses. In one embodiment, the solution contains 0.01 to 0.5 weight percent sodium chloride. The solutions

employed in the present invention may also include surfactants such as a polyoxyethylene-polyoxypropylene nonionic surfactant which, for example, can be selected from the group of commercially available surfactants having the name poloxamine or poloxamer, as adopted by The CTFA International Cosmetic Ingredient Dictionary. The poloxamine surfactants consist of a poly(oxypropylene)-poly(oxyethylene) adduct of ethylene diamine having a molecular weight from about 7,500 to about 27,000 wherein at least 40 weight percent of said adduct is poly(oxyethylene), has been found to be particularly advantageous for use in conditioning contact lenses when used in amounts from about 0.01 to about 15 weight percent. Such surfactants are available from BASF Wyandotte Corp., Wyandotte, Mich., under the registered trademark "Tetronic" TETRONIC. The poloxamers are an analogous series of surfactants and are polyoxyethylene, polyoxypropylene block polymers available from BASF Wyandotte Corp., Parsippany, N.J. 07054 under the trademark "Pluronics" PLURONIC.

Please replace paragraph [0027] of the specification with the following amended paragraph:

[0027] Additional compatible surfactants that are known to be useful in contact wetting or rewetting solutions can be used in the solutions of this invention. The surfactant should be soluble in the lens care solution and non-irritating to eye tissues. Satisfactory non-ionic surfactants include polyethylene glycol esters of fatty acids, e.g. coconut, polysorbate, polyoxyethylene or polyoxypropylene ethers of higher alkanes (C₁₂-C₁₈). Examples of the class include polysorbate 20 (available from ICI Americas Inc., Wilmington, Del. 19897 under the trademark ~~Tween® 20~~ TWEEN 20), polyoxyethylene (23) lauryl ether (BRIG 35 ~~Brij® 35~~), polyoxyethylene (40) stearate (MYRJ 52 ~~Myrj® 52~~), polyoxyethylene (25) propylene glycol stearate (ATLAS G2612 ~~Atlas® G 2612~~). ~~Brij® 35, Myrj® 52 and Atlas® G 2612~~ BRIJ 35, MYRJ 52 and ATLAS G 2612 are trademarks of, and are commercially available from, ICI Americas Inc., Wilmington, Del. 19897.

Please replace paragraph [0028] of the specification with the following amended paragraph:

[0028] Various other surfactants suitable for in the invention can be readily ascertained, in view of the foregoing description, from McCutcheon's Detergents and Emulsifiers, North American Edition, McCutcheon Division, MC Publishing Co., Glen Rock, N.J. 07452 and the

CTFA International Cosmetic Ingredient Handbook, Published by The Cosmetic, Toiletry, and Fragrance Association, Washington, D.C. however, the preferred surfactants are commercially available surfactants sold under the trademark ~~eremaphor~~tm CREMOPHOR by BASF and which are polyoxyethoxylated castor oils.

Please replace paragraph [0030] of the specification with the following amended paragraph:

[0030] A set of aqueous solutions containing Pluronie PLURONIC F127 (0.1%) and glycerin (2%) ~~was were~~ prepared and the pH was adjusted to pH 7.65. Polyhexamethylene biquanide (PHMB) was added to half of this solution to yield a final concentration of 1 ppm. Another set of aqueous solutions containing hydrogen peroxide (60 ppm), Pluronie® F127 PLURONIC F127 (0.1%) and glycerin (2.3%) was prepared the pH was adjusted to pH 7.35. Polyhexamethylene biquanide (PHMB) was added to half of this solution to yield a final concentration of 1 ppm.

Please replace paragraph [0035] of the specification with the following amended paragraph:

[0035] Formulations were prepared by dissolving L-histidine or Bis-Tris Propane in water. The pH of the solutions were adjusted to 7.3 with 1N hydrochloric acid. Hydrogen peroxide, Dequest® 2010 DEQUEST 2010 and polyhexamethylenebiguanide HCl (PHMB) were added to these solutions. The formulations were diluted to volume with water. Each of these solutions were tested for their activity against *C. albicans* (ATCC 10231) following a two hour exposure. The activity is expressed as a log reduction from the initial inoculum. The compositions, concentrations and activity of each of the solutions are summarized in the following table.

Log Reduction	Preservative	Buffer	Hydrogen Peroxide	<u>Dequest 2010</u>
1.59	Bis-Tris Propane	none	none	0.006%
	0.2%			
2.05	Bis-Tris Propane	none	0.006%	0.006%

		0.2%		
1.25	L-histidine 0.2%	none	none	0.006%
1.85	L-histidine 0.2%	none	0.006%	0.006%

Please replace paragraph [0037] of the specification with the following amended paragraph:

[0037] Formulations were prepared by dissolving L-histidine, Bis-Tris Propane, or Tricine in water. The pH of the solutions were adjusted to 7.3 with 1N hydrochloric acid. Glycerin, hydrogen peroxide, ~~Dequest 2010~~ DEQUEST 2010 and polyhexamethylenebiguanide HCl (PHMB) were added to these solutions. The formulations were diluted to volume with water. Each of these solutions were tested for their activity against *C. albicans* (ATCC 10231) following a two hour exposure. The activity is expressed as a log reduction from the initial inoculum. The compositions, concentrations and activity of each of the solutions are summarized in the following table.

Log Reduction	Preservative	Buffer	Glycerin	Hydrogen Peroxide	Dequest 2010 <u>DEQUEST 2010</u>
1.60	PHMB 0.0001%	L-Histidine 0.2%	none	none	none
2.38	PHMB 0.0001%	L-Histidine 0.2%	none	0.006%	none
1.27	PHMB 0.0001%	L-Histidine 0.2%	none	none	0.006%
2.25	PHMB 0.0001%	L-Histidine 0.2%	none	0.006%	0.006%
1.08	PHMB 0.0001%	L-Histidine 0.2%	none	none	0.003%
2.04	PHMB 0.0001%	L-Histidine 0.2%	none	0.006%	0.003%
1.57	PHMB 0.0001%	L-Histidine 0.2%	0.50%	none	none
2.15	PHMB 0.0001%	L-Histidine 0.2%	0.50%	0.006%	none
1.25	PHMB 0.0001%	L-Histidine 0.2%	0.50%	none	0.006%
2.04	PHMB 0.0001%	L-Histidine 0.2%	0.50%	0.006%	0.006%
1.08	PHMB 0.0001%	L-Histidine 0.2%	0.50%	none	0.003%
1.93	PHMB 0.0001%	L-Histidine 0.2%	0.50%	0.006%	0.003%
2.80	PHMB 0.0001%	Bis-Tris Propane 0.2%	none	none	none
3.69	PHMB 0.0001%	Bis-Tris Propane 0.2%	none	0.006%	none

2.20	PHMB 0.0001%	Bis-Tris Propane 0.2%	none	none	0.006%
3.18	PHMB 0.0001%	Bis-Tris Propane 0.2%	none	0.006%	0.006%
2.18	PHMB 0.0001%	Bis-Tris Propane 0.2%	none	none	0.003%
3.05	PHMB 0.0001%	Bis-Tris Propane 0.2%	none	0.006%	0.003%
2.78	PHMB 0.0001%	Bis-Tris Propane 0.2%	0.50%	none	none
3.32	PHMB 0.0001%	Bis-Tris Propane 0.2%	0.50%	0.006%	none
2.29	PHMB 0.0001%	Bis-Tris Propane 0.2%	0.50%	none	0.006%
3.29	PHMB 0.0001%	Bis-Tris Propane 0.2%	0.50%	0.006%	0.006%
2.13	PHMB 0.0001%	Bis-Tris Propane 0.2%	0.50%	none	0.003%
3.31	PHMB 0.0001%	Bis-Tris Propane 0.2%	0.50%	0.006%	0.003%
1.64	PHMB 0.0001%	Tricine 0.2%	none	none	none
2.05	PHMB 0.0001%	Tricine 0.2%	none	0.006%	none
1.16	PHMB 0.0001%	Tricine 0.2%	none	none	0.006%
1.76	PHMB 0.0001%	Tricine 0.2%	none	0.006%	0.006%
1.17	PHMB 0.0001%	Tricine 0.2%	none	none	0.003%
1.78	PHMB 0.0001%	Tricine 0.2%	none	0.006%	0.003%

Please replace paragraph [0038] of the specification with the following amended paragraph:

[0038] The results demonstrate the improved antifungal against *C. albicans* in each paired formulation, when 0.006% hydrogen peroxide is added. The data demonstrates that the increased activity is independent on the presence of ~~Dequest~~ DEQUEST 2010.

Please replace paragraph [0039] of the specification with the following amended paragraph:

[0039] Formulations were prepared by dissolving Tricine, Citric Acid, Bicine, L-histidine, Glycine, or Lysine in water. The pH of the solutions were adjusted to 7.3 with 1N hydrochloric acid. Hydrogen peroxide, ~~Dequest~~ [®] 2010 DEQUEST 2010 and polyhexamethylenebiguanide HCl (PHMB) were added to these solutions. The formulations were diluted to volume with water. Each of these solutions were tested for their activity against *C. albicans* (ATCC 10231) following a two hour exposure. The activity is expressed as a log

reduction from the initial inoculum. The compositions, concentrations and activity of each of the solutions are summarized in the following table.

Log Reduction	Preservative	Buffer	Hydrogen Peroxide	Dequest 2010
1.90	PHMB 0.0001%	Tricine 0.2%	none	none
2.09	PHMB 0.0001%	Tricine 0.2%	0.006%	0.003%
0.25	PHMB 0.0001%	Citric Acid 0.2%	none	none
0.70	PHMB 0.0001%	Citric Acid 0.2%	0.006%	0.003%
2.01	PHMB 0.0001%	Bicine 0.2%	none	none
2.47	PHMB 0.0001%	Bicine 0.2%	0.006%	0.003%
2.01	PHMB 0.0001%	Histidine 0.2%	none	none
2.42	PHMB 0.0001%	Histidine 0.2%	0.006%	0.003%
1.94	PHMB 0.0001%	Glycine 0.2%	none	none
2.89	PHMB 0.0001%	Glycine 0.2%	0.006%	0.003%
2.69	PHMB 0.0001%	Lysine 0.2%	none	none
2.84	PHMB 0.0001%	Lysine 0.2%	0.006%	0.003%

Please replace paragraph [0041] of the specification with the following amended paragraph:

[0041] Formulations were prepared by dissolving Bis-Tris Propane, L-histidine, or Tricine in water. The pH of the solutions were adjusted to 7.3 with 1N hydrochloric acid. The tonicity agent, hydrogen peroxide, Dequest 2010 DEQUEST 2010 and polyhexamethylenebiguanide HCl (PHMB) were added to these solutions. The formulations were diluted to volume with water. Each of these solutions were tested for their activity against *C. albicans* (ATCC 10231)

following a two hour exposure. The activity is expressed as a log reduction from the initial inoculum. The compositions, concentrations and activity of each of the solutions are summarized in the following table.

Log Reduction	Preservative	Buffer	Tonicity Agent	Wetting Agent	Peroxide	Hydrogen Dequest <u>DEQUES</u> <u>T 2010</u>
3.85	PHMB	Bis-Tris Propane	none	Cremophor	none	none
	0.0001%	0.2%		<u>CREMOPHOR</u>		
				RH 40		
4.70	PHMB	Bis-Tris Propane	none	Cremophor	0.006%	0.003%
	0.0001%	0.2%		<u>CREMOPHOR</u>		
				RH 40		
2.42	PHMB	L-Histidine 0.2%	none	Cremophor	none	none
	0.0001%			<u>CREMOPHOR</u>		
				RH 40		
3.34	PHMB	L-Histidine 0.2%	none	Cremophor	0.006%	0.003%
	0.0001%			<u>CREMOPHOR</u>		
				RH 40		
2.17	PHMB	Tricine	none	Cremophor	none	none
	0.0001%			<u>CREMOPHOR</u>		
				RH 40		
2.69	PHMB	Tricine	none	Cremophor	0.006%	0.003%
	0.0001%			<u>CREMOPHOR</u>		
				RH 40		
3.70	PHMB	Bis-Tris Propane	glycerin 3%	Cremophor	none	none
	0.0001%	0.2%		<u>CREMOPHOR</u>		
				RH 40		

4.40	PHMB	Bis-Tris Propane	glycerin 3%	<u>Cremophor</u>	0.006%	0.003%
	0.0001%	0.2%		<u>CREMOPHOR</u>		
				RH 40		
2.19	PHMB	L-Histidine 0.2%	glycerin 3%	<u>Cremophor</u>	none	none
	0.0001%			<u>CREMOPHOR</u>		
				RH 40		
2.94	PHMB	L-Histidine 0.2%	glycerin 3%	<u>Cremophor</u>	0.006%	0.003%
	0.0001%			<u>CREMOPHOR</u>		
				RH 40		
2.19	PHMB	Tricine	glycerin 3%	<u>Cremophor</u>	none	none
	0.0001%			<u>CREMOPHOR</u>		
				RH 40		
2.45	PHMB	Tricine	glycerin 3%	<u>Cremophor</u>	0.006%	0.003%
	0.0001%			<u>CREMOPHOR</u>		
				RH 40		
2.19	PHMB	L-Histidine 0.2%	propylene	<u>Cremophor</u>	none	none
	0.0001%		glycol 3%	<u>CREMOPHOR</u>		
				RH 40		
2.95	PHMB	L-Histidine 0.2%	propylene	<u>Cremophor</u>	0.006%	0.003%
	0.0001%		glycol 3%	<u>CREMOPHOR</u>		
				RH 40		
4.40	PHMB	Bis-Tris Propane	sorbitol 5%	<u>Cremophor</u>	none	none
	0.0001%	0.2%		<u>CREMOPHOR</u>		
				RH 40		
4.70	PHMB	Bis-Tris Propane	sorbitol 5%	<u>Cremophor</u>	0.006%	0.003%
	0.0001%	0.2%		<u>CREMOPHOR</u>		
				RH 40		
3.36	PHMB	L-Histidine 0.2%	sorbitol 5%	<u>Cremophor</u>	none	none
	0.0001%			<u>CREMOPHOR</u>		
				RH 40		
3.92	PHMB	L-Histidine 0.2%	sorbitol 5%	<u>Cremophor</u>	0.006%	0.003%

		0.0001%		<u>CREMOPHOR</u>		
				RH 40		
2.54	PHMB	L-Histidine 0.2%	inositol 5%	Cremophor RH	none	none
		0.0001%		40		
3.08	PHMB	L-Histidine 0.2%	inositol 5%	Cremophor	0.006%	0.003%
		0.0001%		<u>CREMOPHOR</u>		
				RH 40		

Please replace paragraph [0042] of the specification with the following amended paragraph:

[0042] The data shows that the addition of 0.006% hydrogen peroxide to polyhexamethylene biguanide provides increased antifungal activity against *C. albicans*. Consistent results were found in the presence of Cremophor CREMOPHOR RH40 with histidine, tricine, Bis-Tris Propane, glycerin, propylene glycol, and sorbitol.